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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/686,737 | 10/10/2000 | Junquan Xu | ART-00102.P.1 | 7112 |

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| EXAMINER | |
|---|---|
| DO, PENSEE T | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1641 | 11 |

DATE MAILED: 11/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/686,737 | XU ET AL. | |
| | Examiner | Art Unit | |
| | Pensee T. Do | 1641 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *31 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *61-99* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *61-99* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

### *Amendment Entry & Claim Status*

The amendment filed on July 14, 2003 has been acknowledged and entered as paper no. 10.

Claims 61-99 are pending.

### *Withdrawn Rejection(s)*

Rejections under 35 USC 112, 2nd paragraph, 102, and 103 are withdrawn herein.

### *Newgrounds of Rejection(s)*

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 61-99 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 61 is unclear in reciting "selectively modifies" in line 2. How is the solution modified or alter or tune-in to "selectively" modify the dielectric property of at least one component of the sample?

Claim 64 is also indefinite in reciting "selectively lyses". Does the solution lyses certain kind of red blood cells? If so, what are the kinds of red blood cells that are being lysed. See also claim 75 for the same problem.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 61, 62, 64, 65, 66, 70, 74-76, are rejected under 35 U.S.C. 102(e) as being anticipated by Ryan (US 6,200,500).

Ryan teaches a solution containing glycerol. Such solution is combined with a solution of blood regulates the osmolarity of blood cell solution from 300 mosm to about 150 mosm.(see col. 6, lines 49-61). Claim 61, part (c ) is a function of how much sample is mixed with the claimed solution which is not given any patentably weight because such limitation is an intended use of the claimed sample solution. Since the sample solution recites as comprising nothing other than glycerol (claim 65), then a solution containing glycerol would inherently have the property of modifying at least one dielectric property of at least one component in the sample and has conductivity such that one or more moieties of said sample can be separated using dielectrophoresis forces. Thus, the solution can also lyses red blood cells. Claims 70, 74-76 are inherent for a method of separating sample mixture using dielectrophoresis force since glycerol has inherent property of conductivity such that one ore more moieties of the sample in which glycerol is mixed with can be separated using dielectrophoresis forces.

Claims 61, 63, 70-75, 77-78, 88, are rejected under 35 U.S.C. 102(e) as being anticipated by Becker et al. (US 5,993,630).

Becker teaches a method of fractionating using conventional dielectrophoresis and field flow fractionation. The method comprises introducing a fluid that carries particulate matter through a separation chamber; separating one or more moieties of said sample using dielectrophoresis forces. The fluid can be a mixture of dextrose and sucrose or switterionic solutions. (see col. 18, lines 18-25). In another embodiment, a sample of HL-60 cells cultured in a medium of FBS 22 mM HEPES is added to a chamber of an apparatus for field flow fractionation. (see col. 21, lines 30-35). The moieties are cells such as white blood cells, tumor cells, etiological agents, blood. (see col. 14, lines 13-38). Regarding the limitation in part (c ) of claim 61, it is not given any patentably weight because such limitation is an intended use of the sample solution as a result of how much sample is mixed with the claimed sample solution. Thus, such limitation is not part of the claimed sample solution.

Claims 61, 63, 70-74, 79-82, 84-87 are rejected under 35 U.S.C. 102(e) as being anticipated by Cheng et al. (US 6,280,590).

Cheng teaches devices and methods for performing channel-less separation of cell particles by dielectrophoresis, separation of desired components from crude mixtures such as cell lysates, and/or enzymatic reaction of such lysates, all of which can be conducted on a single bioelectronic chip. The bioelectronic chip is a microfabricated silicon chip on a printed circuit board and a flow cell mounted on the chip to form a flow chamber. The chip includes a plurality of circular microelectrodes which are preferably

coated with a protective permeation layer which prevents direct contact between any electrode and a sample introduced into the flow chamber. (see col. 4, line 50-col. 5, line 15). One example method of using such device includes preparation of a cell sample for introduction (e.g. suspension in a cell separation buffer) and subsequent dielectrophoresis; introduction of the sample into the flow cell (e.g. via pumping); subjecting the sample to an electric field to dielectrophoretically separate the desired cells from the sample. A cell separation buffer comprising 0.05x TBE (4.5 uM Tris, 4.5 uM boric acid, 0.1 uM EDTA, pH 8.2), 250 mM sucrose, pH 8.2 , was prepared. The conductivity of the buffer was 114 uS/cm measured by an Accumet pH meter 50. The conductivity under which cell separation was carried out was chosen carefully to ensure that the desired cells were subjected to positive electrophoresis and all normal human blood cells were subjected to negative dielectrophoresis. (see col. 8, line 60-col. 9, line 10). In another embodiment, to perform the dielectrophoretic separation of *E. coli* cells from blood cells in the cell culture, an unused cartridge was employed. The chip of the cartridge was first washed by pumping a separation buffer (sample solution) from a sample/buffer reservoir through a tubing and flow cell. Next, the cell culture was pumped into the flow cell and the pump was switched off. The entire array of electrodes were addressed in a checkerboard bias format providing field maxima at each electrode and field minima in the areas between the electrodes. (see col. 10, lines 40-50). After separation, assay is carried out to detect the desired component in the separated cells. Thus, binding agent must be coupled to one component in the sample for the assay. (see col. 11, line 62-col. 12, line 8). Regarding the limitation in part (c ), osmolarity

range, of claim 61, it is not given any patentably weight because such limitation is an intended use of the sample solution as a result of how much sample is mixed with the claimed sample solution. Thus, such limitation is not part of the claimed sample solution.

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 61-63 are rejected under 35 U.S.C. 102(b) as being anticipated by Products for Molecular Biology, Molecular Sigma Biology 1992, pp.83-86.

Molecular Sigma Biology teaches sample solutions such as EDTA (page 83), HEPES (p. 84), MOPS, MOPS-EDTA sodium acetate (p. 85), and PIPES (p. 86). According to the present specification, the claimed sample solution can be any zwitterionic compounds such as PIPES, HEPES, MOPS, or EDTA. Thus, if Molecular Sigma Biology teaches these reagents, then these solution would inherent properties such as selectively modifies at least one dielectric property of at least one component of the sample and has a conductivity such that one or more moieties of said sample can be separated using dielectrophoretic forces. Regarding the limitation in part (c ), osmolarity range, of claim 61, it is not given any patentably weight because such limitation is an intended use of the sample solution as a result of how much sample is mixed with the claimed sample solution. Thus, such limitation is not part of the claimed sample solution.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

. Claims 67 and 68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ryan (US 6,200,500) in view of Horan et al. (US 4,783,401).

Ryan has been discussed above.

However, Ryan fails to teach the sample solution comprising sucrose, mannose, mannitol or sorbitol.

Horan et al. teach a cell labeling method performed in a medium that is non-lethal to cells. Such medium contains osmolarity regulating agents such as glucose, sucrose and sugar-alcohols such as mannitol, glycerol. (see col. 4, lines 24-35).

It would have been obvious to one of ordinary skills in the art to substitute the osmolarity regulating agents such as sucrose or mannitol taught in Horan for the glycerol in Ryan since sucrose and mannitol are considered osmolarity regulating agents, solution containing any of these sugars would have the same properties as one containing glycerol. Cell labeling can be safely performed in solution containing such sugars without causing damage to the cells.

Claim 83 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cheng et al. (US 6,280,590).

Cheng has been discussed above.

However, Cheng fails to teach adding the sample to the chamber before the sample solution is added to said chamber.

It would have been obvious to alternate the order of adding the sample and the sample solution to the flow chamber because regardless of the order in which the sample or sample solution is added to the chamber, the result would be the same. No unexpected result would be achieved.

***Remarks***

Claims 89-99 are free of prior arts

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 703-308-4398. The examiner can normally be reached on Monday-Friday, 7:00-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 703-305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641

Pensee T. Do
Patent Examiner
October 16, 2003